OPEN PEER REVIEW

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Peer Review Report for "Air Pollution and Hospital Admission for Epilepsy in Kerman, Iran"

Author(s): Mohammad Amin Farahmandfard, Hossein Ali Ebrahimi, Narges Khanjani, Moghaddameh Mirzaee

Review Timeline:

Submit Date: 4 Apr 2022
Revised Date: 12 Jun 2022
Accepted Date: 29 Jun 2022

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Eshagh Barfar: Reviewer | **Revision** (0) — 15 Apr 2022

Dear Associate Editor,
The manuscript needs minor revisions as follows:
1. When an acronym is mentioned in the paper, the acronym must be preceded by the full phrase for the first time. This is not considered for the CNS in line 2 of the Background section.
2. Prevalence of epilepsy in Iran should be added to the last paragraph of the Background section.
3. The type of study should be added at the beginning of the Method section.
4. The data collection tools, inclusion and exclusion criteria, and the type of sampling should be clearly explained in the method section.
5. Study limitations should be added to the Discussion section.
6. According to the results of this study, what advice do you have for health policy makers?

Best Regards

Hossein Ansari: Reviewer | **Revision** (0) — 18 Apr 2022

Why have not used the author from Poisson regression or time series analysis to manage this data?
The authors should explain briefly the GAM method
The explanation for table 2 is not complete. It is not clear what these means belong to or what meant of “Attack” and its distribution based on sex and age is
It is not clear how the authors have evaluated the accuracy of the model and residuals
The trend of data should be presented using a suitable chart

Majid Sartipi: Reviewer | **Revision (0)** 21 Apr 2022

Dear author:
- Explain words that are not common, such as PM10, PM2.5.
- In line 31 you used the term Rate Ratio, while in the rest of the text, the Relative Risk is used. Please correct.
- In line 44, the sum of 57.7 and 44.3 is greater than 100 (102)
- In the results, even in significant cases, the RR values are so small that you have to list up to 4 decimal places. There is no explanation for justifying these weak relationships. It seems that there is a need for explanation and justification in this regard.
- About half of the pages of the article are devoted to tables. Is it necessary to insert such long tables? Is it not possible to summarize it?
Sincerely yours

Hossein Ansari: Associate Editor | **Revision (0)** 24 Apr 2022

First reviewers’ comments
Dear author:
- Explain words that are not common, such as PM10, PM2.5.
- In line 31 you used the term Rate Ratio, while in the rest of the text, the Relative Risk is used. Please correct.
- In line 44, the sum of 57.7 and 44.3 is greater than 100 (102)
- In the results, even in significant cases, the RR values are so small that you have to list up to 4 decimal places. There is no explanation for justifying these weak relationships. It seems that there is a need for explanation and justification in this regard.
- About half of the pages of the article are devoted to tables. Is it necessary to insert such long tables? Is it not possible to summarize it?
Sincerely yours

Second reviewer’s comments
Why have not used the author from Poisson regression or time series analysis to manage this data?
The authors should explain briefly the GAM method
The explanation for table 2 is not complete. It is not clear what these means belong to or what meant of “Attack” and its distribution based on sex and age is
It is not clear how the authors have evaluated the accuracy of the model and residuals
The trend of data should be presented using a suitable chart

Third reviewers' comments

Dear Associate Editor,
The manuscript needs minor revisions as follows:
1. When an acronym is mentioned in the paper, the acronym must be preceded by the full phrase for the first time. This is not considered for the CNS in line 2 of the Background section.
2. Prevalence of epilepsy in Iran should be added to the last paragraph of the Background section.
3. The type of study should be added at the beginning of the Method section.
4. The data collection tools, inclusion and exclusion criteria, and the type of sampling should be clearly explained in the method section.
5. Study limitations should be added to the Discussion section.
6. According to the results of this study, what advice do you have for health policy makers?
Best Regards

Ramazan Mirzaei: EIC | **Revision (0)** 27 Apr 2022

Dear Author

According to reviewer comments, the manuscript needs "Major revision".
Best Regards

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear Editor,
These changes have been made in the article:

Reviewer 1

Why have not used the author from poisson regression or time series analysis to manage thus data?
Time series models are used to predict the trend of pollutants and dependent variables. However, the purpose of our study was only to investigate the relation between pollutants and epileptic seizures and we did not predict any trends or changes.
In this study, Generalized Additive Model (GAM) which are a special type of Poisson regression were used to measure the relation between air pollutants and epileptic seizures. GAM is widely used in studies of air pollution and health outcome studies. This model can adjust the effect of nonlinear confounders such as seasonal and climate changes.

The authors should explain briefly about the GAM method.
Generalized Additive Models (GAM) similar to the equation below were used for estimating Rate Ratios (RR), with up to 7 day lags. The time unit used was day. GAM has been used in many air pollution and health studies. This method can adjust for nonlinear confounding effects such as seasonal changes and meteorological variables.

$$Y_t \quad Poisson(\mu_t)$$
$$\log \mu_t = \alpha + \sum \beta_i (X_i) + \sum S_j (X_j)$$

Where Yt denotes the daily number of epilepsy relapse in total, male, female and age groups. βi is the coefficient for air pollutants (Xi) and denotes the log of the Relative Risk, and Sj (Xj) are the smoothing functions of meteorological variables (temperature and relative humidity).

The explanation for table 2 is not complete. It is not clear that what these means are belong to or what meant of “Attack” and its distribution based on sex and age is
The descriptive statistics in the last rows were about the number of epilepsy admissions and because they were not important we deleted them.

It is not clear that how the authors have evaluated the accuracy of the model and residuals the trend of data should be presented using a suitable chart.
In this study, similar to other studies examining the relation between air pollutants and health consequences (4-1), we only examined the association of epileptic seizures with air pollutants and we did not need to predict or study the trend of the data.

Reviewer 2

When an acronym is mentioned in the paper, the acronym must be preceded by the full phrase for the first time. This is not considered for the CNS in line 2 of Background section.
We added the full phrase “Central Nervous System” in line 2.

Prevalence of epilepsy in Iran should be added to the last paragraph of the Background section.
We added “the prevalence of epilepsy in Kerman city was 7.87 per 1000 people in 2011” in the last paragraph of the background.

The type of study should be added at the beginning of the Method section.

We added that “this was an ecological study”.

The data collection tools, inclusion and exclusion criteria and the type of sampling should be clearly explained in the method section.
We did not do data collection. Data was inquired from the organizations mentioned in the article.

Study limitations should be added to the Discussion section.
We added some limitations on page 13.

According to the results of this study, what advice do you have for health policy makers?
This study emphasizes the need to control and reduce ambient air pollutants in Kerman.

Reviewer 3

Explain words that are not common, such as PM10, PM2.5.
These abbreviations are very well known in air pollution research. Nevertheless, we added the explanation to the text.

In line 31 you used the term Rate Ratio, while in the rest of the text the Relative Risk is used.
We edited this and we used “Rate Ratio” instead of Relative Risk everywhere.

In line 44, the sum of 57.7 and 44.3 is greater than 100 (102).
Sorry for the typo. 894 epilepsy admissions occurred in Kerman, in which 498 (**55**.7%) cases were male and 396 (44.3%) were female.

In the results, even in significant cases, the RR values are so small that you have to list up to 4 decimal places. There is no explanation for justifying these weak relationships. It seems that there is a need for explanation and justification in this regard.
In most ecological studies that have examined the effect of air pollution, the rate ratio is not a big number (2-7). A number like 1.0051, means a half percent increase in MS attacks per each 1 unit increase in CO and 10-unit increase in all other pollutants. In our study, we only had a total of 894 attacks, and the results are reasonable.

About half of the pages of the article are devoted to tables. Is it necessary to insert such long tables? Is it not possible to summarize it?
The long tables are because we have to examine at least up to seven day lags. Other similar studies (3-4, 8-9) have also examined the increase in attacks up to seven days lag of exposure to pollutants. This is because air pollution has lagged effects.

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2. Jeanjean M, Bind MA, Roux J, Ongagna JC, De Sèze J, Bard D, Leray E. Ozone, NO2 and PM10 are associated with the occurrence of multiple sclerosis relapses. Evidence from seasonal multi-pollutant analyses. Environmental research. 2018 May 1;163:43-52.

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Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Hossein Ansari: Associate Editor | **Revision** (**1**) — 11 May 2022

The authors have revised the manuscript based on the reviewers' comments.

Hossein Ansari: Reviewer | **Revision** (**1**) — 23 May 2022

The authors have revised the manuscript based on the reviewers' comments.

Eshagh Barfar: Reviewer | **Revision** (**1**) — 28 May 2022

Dear Associate Editor,
Although some issues have been fixed, the manuscript still needs to be addressed:
1. The prevalence of epilepsy in Iran (as a whole) also should be added to the last paragraph of the Background section.
2. The data collection checklist (or tool), inclusion and exclusion criteria and the type of sampling should be clearly explained in the method section.
3. According to the results of this study, what practical advice do you have for health policy makers?
Best regards

Hossein Ansari: Associate Editor | **Revision** (**1**) — 30 May 2022

Although some issues have been fixed, the manuscript still needs to be addressed:
1. The prevalence of epilepsy in Iran (as a whole) also should be added to the last paragraph of the Background section.
2. The data collection checklist (or tool), inclusion and exclusion criteria and the type of sampling should be clearly explained in the method section.
3. According to the results of this study, what practical advice do you have for health policy makers?
Best regards

Ramazan Mirzaei: EIC | **Revision** (**1**) — 5 Jun 2022

Dear Author
Thanks for submitting your valuable manuscript to the journal. As a result of this, we would like to inform you that the review of your manuscript is finished, and based on the editorial

decision, you need to do a "Minor Revision" on your manuscript. Even though this manuscript has enough quality to enter the review process, it needs some significant (minor) revisions in some points of view.

Best Regards

OPEN PEER REVIEW

Revision (2)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear Editor,
These changes have been made in the article:

:Reviewer 2
Prevalence of epilepsy in Iran should be added to the last paragraph of the Background .1 .section
We added “The prevalence of epilepsy in Kerman city was 7.87 per 1000 people in 2011 (1). A recent review estimated that there are about 840,000 people with active epilepsy living in .Iran and its prevalence in Iran is 1% (2).” in the last paragraph of the background

2. The data collection tools, inclusion and exclusion criteria and the type of sampling should be clearly explained in the method section.
We did not do data collection. Data was inquired from the organizations mentioned in the article. We did not do sampling. All patient data was included.

3. According to the results of this study, what advice do you have for health policy makers?
We added this to the conclusion: “This study emphasizes the need to control and reduce ambient air pollutants in Kerman. Additionally, Epilepsy patients should better stay away from exposure to polluted air. Staying at home on polluted days or residing in areas with less air pollution might be an option. “

References

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2. Asadi-Pooya AA, Simani L. Epilepsy syndromes in Iran: A systematic review. Acta Neurologica Scandinavica. 2021 May; 143 (5):475-80.

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Revision (2)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Hossein Ansari: Associate Editor | **Revision** (2) 18 Jun 2022

The authors have revised the manuscript based on the reviewers' comments.

Ramazan Mirzaei: EIC | **Revision** (2) 29 Jun 2022

Dear Author

According to reviewer comments, we congratulate inform you that your article has been accepted for publication in this journal and we thank you for trusting us. As an expert in the field, you are best placed to explain why your article is exciting or impactful to a broader so if you fulfill your other commitments promptly, your article will be published in this journal at the appointed time.

Kind regards